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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,987	02/13/2002	Maria Alexandra Glucksmann	MPI98-047CP2DV2M	9969
30405	7590	08/10/2005	EXAMINER	
MILLENNIUM PHARMACEUTICALS, INC. 40 Landsdowne Street CAMBRIDGE, MA 02139			BRANNOCK, MICHAEL T	
			ART UNIT	PAPER NUMBER
			1649	

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/075,987

Applicant(s)

GLUCKSMANN ET AL.

Examiner

Michael Brannock

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 May 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24,25 and 33-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24,25 and 33-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 July 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>040405</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Status of Application: Claims and Amendments

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

Applicant is notified that the amendments put forth on 5/23/05, have been entered in full.

Response to Amendment

Applicant is notified that any outstanding objection or rejection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's amendments and persuasive arguments regarding the rejection under 35 USC 101.

Information Disclosure Statement

The information disclosure statement filed 4/4/05 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP 609 because citation B11 lacks sufficient description so as to lead the reader to the cited documents. Thus citation B11 was not considered.

Applicant argues that a complete description of the references in July 30, 2002 IDS is provided in supplemental information disclosure statement filed 4/4, 2005. This argument has been fully considered but not deemed persuasive.

The 4/4/2005 IDS also fails to comply for the essentially the same reason as that of the July 30, 2005 IDS. As set forth previously regarding the objection to the specification, the attempt to incorporate subject matter into this application by reference to active Internet sites (i.e., hyperlinks) is improper because such web sites are constantly being changed and updated.

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A change or update of the web site would automatically raise the issue of new matter, because the updated information was not known to the inventors at the time of the filing of the instant specification. Also, the organization, views and accuracy of the information contained on commercial web sites is not under the control of the PTO. Thus, one could not be sure that the material on the website at any time in the future was the same material that applicant requests the examiner to consider. Thus, this website has not been considered by the examiner. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP 609 & C(1).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24, 25, 33-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons:

The claims require detection of “modulation” of particular activities. It is unclear what limitations are placed on the claim by the presence of the word “modulation”, i.e. are there properties that are to be detected other than inhibition or activation as in claims 39 and 40?

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24, 25, 33-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. .

The claims require the step of detecting stimulation or inhibition of the activity of the 14273 polypeptide. As is it commonly understood, the activity of a GPCR is induced by binding to an external ligand, yet no ligand has been identified by the specification. It is well established that it may take years of intensive trial and error experimentation to find a ligand for a GPCR. Nor has the specification taught what G-protein(s) couple to the receptor, or what fragments provide any activity, and nor has the specification taught what particular activities could be detected. The specification has merely provided a generalized list of activities that certain GPCRs have been shown to have. No particular activities are asserted to be associated with the 14273 receptor activity. Thus the artisan is left to perform extensive trial and error research and investigation in the hope of finding a ligand, finding a G-protein, and finding a specific activity that can be measured.

“Tossing out the mere germ of an idea does not constitute enabling disclosure... [R]easonable detail must be provided in order to enable members of the public to understand and carry out the

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invention.” *Genentech, Inc. v. Novo Nordisk Inc.*, 108 F.3d 1361, 1366, 42 U.S.P.Q.2d 1001, 1005 (Fed. Cir. 1997).

Therefore, due to the large quantity of experimentation necessary to try to find a ligand for the polypeptide, to try to find a G-protein, and to try to find an activity in which to measure, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the art which recognizes the difficulty in pairing a ligand with an orphan GPCR, and the breadth of the claims which encompass and an indeterminately large scope of possible activities for the polypeptide of which the claims require knowledge of, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Applicant argues that the art recognizes assays that can be used to identify active 14273 polypeptide without direct knowledge of the ligand or any transduction components. Applicant cites the Barak et al. patent, Barak et al. (1997), and Silvermen et al. 1998 in support of these assertions. These references and arguments has been fully considered but not deemed persuasive. Specifically, Applicant points to the paragraph on page 27500 of Barak et al. for specific support, however Barak et al specifically state in this passage “cellular visualization of the agonist mediated translocation of Barr2-GFP provides a universal measure for detecting the activation of unknown GPCRs”. Thus one would *need* the agonist to actually visualize “the agonist mediated translocation of Barr2-GFP”. The instant specification does teach such an agonist nor where to find such. Barak et al. never used the method to actually identify an agonist of an unknown GPCR. Instead, Barak et al. used some of the most thoroughly studied GPCRs and their well characterized agonists and associated kinase to visualize “the agonist mediated translocation of Barr2-GFP”. Nor do they teach how to identify the endogenous signal

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transduction mediators that are encompassed by the claims. One skilled in the art would not view the invitation to use the method of Barak et al. to try to find agonists etc. of the instant polypeptide to be routine. Rather, it would be viewed as an unreasonably burdensome request to embark on an essentially random trial and error research plan to test any and all molecules and peptides, encompassed by the claims, in the uncertain hope of finding such.

Applicant argues that the specification at pages 10-12 and 32 teaches that the 14273 polypeptide has a variety of specific activities. This argument has been fully considered but not deemed persuasive. The skilled artisan appreciates that the specification simply presents the equivalent of a laundry list of second messenger systems that the family of GPCRs is known to utilize. The specification does not assert that the 14273 polypeptide has any particular activity.

Claims 24, 25, 33-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims require that the methods be practiced under conditions suitable for modulation of the 14273 activity. As is it commonly understood, the activity of a GPCR is induced by binding to an external ligand, yet no ligand has been identified by the specification. It is well established that it may take years of intensive trial and error experimentation to find a ligand for a GPCR. Nor has the specification taught what G-protein(s) couple to the receptor, or what

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fragments provide any activity, and nor has the specification taught what particular activities could be detected. The specification has merely provided a generalized list of activities that certain GPCRs have been shown to have. No particular activities are asserted to be associated with the 14273 receptor activity. Thus one skilled in the art would not recognize that applicant was in possession of these fundamentals, enumerated above, required to practice the claimed invention.

Applicant's arguments regarding the prior art and Barak et al., in particular, have been addressed above. Applicant argues that because the claims are drawn to a method and not to fragments of the polypeptide then the assertion that the specification has not taught what fragments provide activity is moot with regard to the instant rejection. This argument has been fully considered but not deemed persuasive. In order to be in possession of the claimed method, one would need to know what fragments would work because they are required by the claims.

Applicant argues that the specification at pages 10-12 and 32 teaches that the 14273 polypeptide has a variety of specific activities. This argument has been fully considered but not deemed persuasive. The skilled artisan appreciates that the specification simply presents the equivalent of a laundry list of second messenger systems that the family of GPCRs is known to utilize. The specification does not assert that the 14273 polypeptide has any specific activity. In order for one to be in possession of the claimed invention, one would need to know what particular activities to measure. A thorough reading of the instant specification by one skilled in the art would indicate to that artisan that the instant inventors did not know what particular activities the 14273 polypeptide has at the time the application was filed, and were therefore not in possession of that which is being claimed.

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Conclusion

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX months.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

**ELIZABETH KEMMERER
PRIMARY EXAMINER**

MB

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August 8, 2005